FEB 05 2004

Image AF 1600

PTO/SB/21 (01-03)
Approval for use through 04/30/2003. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/755,016
Filing Date	Jan 5, 2001
First Named Inventor	Walke, D. Wade
Art Unit	1652
Examiner Name	C. Fronda
Total Number of Pages in This Submission: 17	Attorney Docket Number: LEX-0114-USA

ENCLOSURES *(check all that apply)*

- [ ] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment / Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [x] Appeal Communication to Group ***(Appeal Notice, Brief, Reply Brief)***
- [ ] Proprietary Information
- [ ] Status Letter
- [x] Other Enclosure(s) *(please identify below):*
  - Return Postcard

Remarks

FILED IN TRIPLICATE

Customer # 24231

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual	Lexicon Genetics Incorporated Lance K. Ishimoto Reg. No. 41,866
Signature	Lance K. Ishimoto by David W. Hibler DAVID W. HIBLER REG. NO. 41,071
Date	February 4, 2004

CERTIFICATE OF TRANSMISSION/MAILING

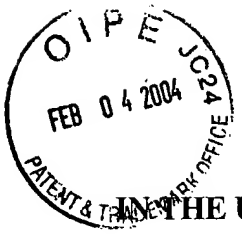
I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as Express Mail Label # EV 173548201 US in an envelope addressed to:

Mail Stop: Appeal Brief - Patents, USPTO, PO Box 1450, Alexandria, VA 22313-1450 on this date: February 4, 2004

Typed or printed	Michelle Klein		
Signature	Michelle Klein	Date	February 4, 2004

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents. Washington, DC 20231.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Walke *et al.*		
Serial No.:	09/755,016	Group Art Unit:	1652
Filed:	01/05/2001	Examiner:	C. Fronda
For:	Novel Human Proteases and Polynucleotides Encoding the Same	Attorney Docket No.:	LEX-0114-USA

REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TABLE OF CONTENTS

APPEAL BRIEF

Sir:

Appellants hereby submit an original and two copies of this Reply Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Examiner's Answer mailed on December 4, 2003. This Reply Brief is timely submitted, and Appellants believe no fees are due in connection with this Reply Brief. However, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

Appellants agree with the Examiner's assertion that "(a) statement identifying the real party in interest is contained in the brief" (Examiner's Answer at page 1).

II. RELATED APPEALS AND INTERFERENCES

Appellants agree with the Examiner's assertion that "(t)he brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief" (Examiner's Answer at page 2).

III. STATUS OF THE CLAIMS

Appellants agree with the Examiner's assertion that "(t)he statement of the status of the claims contained in the brief is correct" (Examiner's Answer at page 2).

IV. STATUS OF THE AMENDMENTS

Appellants agree with the Examiner's assertion that "(t)he appellant's statement of the status of amendments after final rejection contained in the brief is correct" (Examiner's Answer at page 2).

V. SUMMARY OF THE INVENTION

Appellants agree with the Examiner's assertion that "(t)he summary of invention contained in the brief is correct" (Examiner's Answer at page 2).

VI. ISSUES ON APPEAL

Appellants agree with the Examiner's assertion that "(t)he appellant's statement of the issues in the brief is correct" (Examiner's Answer at page 2).

VII. GROUPING OF THE CLAIMS

Appellants disagree with the Examiner's assertion that "Appellant's brief includes a statement that claims 1, 2, and 5-10 do not stand or fall together" (Examiner's Answer at page 2). Appellants clearly stated in the Appeal Brief, and reiterate here, that "(f)or the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, associated with the utility rejection, the claims will stand or fall together. For the purposes of the outstanding rejection under 35 U.S.C. § 112, first paragraph, associated with written description, claims 1 and 7-10 will stand or fall together."

VIII. CLAIMS APPEALED

Appellants agree with the Examiner's assertion that "(t)he copy of the appealed claims contained in the Appendix to the brief is correct" (Examiner's Answer at page 2).

IX. PRIOR ART OF RECORD

Appellants agree with the Examiner's assertion that "Attwood et al." and "Ponting" are the only prior art references of record relied on in the currently pending rejections (Examiner's Answer bridging pages 2 and 3).

X. ARGUMENT

A. Do Claims 1, 2 and 5-10 Lack a Patentable Utility?

Appellants do not wish to restate all of the arguments presented in the Appeal Brief concerning the Examiner's allegation that claims 1, 2 and 5-10 lack a patentable utility, and instead incorporate the entirety of Section VIII(A) of the Appeal Brief at this point herein by reference. However, Appellants are compelled to specifically address certain arguments presented in the Examiner's Answer for the record.

Appellants pointed out in the Appeal Brief that the present nucleic acid sequences have utility in forensic analysis, as described in the specification as originally filed (see, for example, page 10, lines 13-24). As described in the specification at page 15, lines 22-29, the presently claimed sequence defines three coding single nucleotide polymorphisms - specifically, a C/T polymorphism at nucleotide position 28 of SEQ ID NO:3, a silent polymorphism that results in a leucine at amino acid position 10 of SEQ ID NO:4; a C/T polymorphism at nucleotide position 55 of SEQ ID NO:3, which can result in a tyrosine or histidine at amino acid position 19 of SEQ ID NO:4; and a G/A polymorphism at nucleotide position 379 of SEQ ID NO:3, which can result in an alanine or threonine at amino acid position 127 of SEQ ID NO:4. Appellants pointed out that as such polymorphisms are the basis for forensic analysis, which in undoubtedly a "real world" utility, the presently claimed sequence must in itself be useful.

In the Examiner's Answer, the Examiner states that "forensic analysis can be useful for determining the presence or absence of polymorphisms which (*sic*) have been demonstrated to exist" (the Examiner's Answer at page 7), but then states that the polymorphic markers **identified** and **described** by Appellants in the specification as originally filed are not useful in forensic analysis because "the instant specification only describes **potential** polymorphisms but not actual polymorphisms" (the Examiner's Answer at page 7, emphasis in original). The Examiner appears to believe that the polymorphic markers **identified** and **described** by Appellants in the specification as originally filed are not "actual" polymorphisms because of the use of the word "can" by Appellants: "the specification states on page 15, lines 22-30: 'the described NHP sequences **can** contain a variety of polymorphisms such as at nucleotide 28 of SEQ ID NO:3 and nucleotide 55 of SEQ ID NO:3 which both can be a C or a T and **can** give rise to silent mutation at corresponding amino acid position 10 of SEQ ID NO:4 or a tyr or his at amino acid position 19 of SEQ

ID NO:4. The described NHP sequences can also contain G-A polymorphisms at nucleotide 379 of SEQ ID NO:3 and nucleotide position 199 of SEQ ID NO:5 which **can** give rise to a corresponding ala or thr at amino acid position 127 of SEQ ID NO:4, or residue 67 of SEQ ID NO:6.' (emphasis added)" (the Examiner's Answer at page 6, emphasis in original).

First, it should be pointed out that the section of the specification quoted by the Examiner refers to "sequences", specifically, the claimed SEQ ID NOS:3 and 4. Appellants respectfully point out that nucleotide and amino acid sequences in and of themselves cannot contain a polymorphism - rather, a polymorphism is a representation of a position in a population of nucleotide sequences that exhibits variability within a number of independent isolates of a given sequence. Thus, any specific nucleotide sequence, for example SEQ ID NO:3, **can** have either the first or the second nucleotide at the polymorphic position, not both. The same holds true for the specifically claimed amino acid sequence (SEQ ID NO:4); the amino acid sequence **can** have either the first or the second amino acid at the polymorphic position, not both. Thus, the word "can", as used by Appellants in this context, means the possibility of the first nucleotide or amino acid or the second nucleotide or amino acid, **not** that the specific polymorphisms **identified** and **described** by Appellants are "potential" polymorphisms.

Second, the use of the term "can" in the context of the statement "the described NHP sequences can contain a variety of polymorphisms such as" those **identified** and **described** by Appellants also means that "the described NHP sequences" **can** contain other polymorphisms in addition to those **identified** and **described** by Appellants, including any previously identified polymorphisms, and any polymorphisms that might be identified in the future. Thus, the word "can", as used by Appellants in this context, means the possibility of the claimed sequences containing other polymorphisms in addition to those **identified** and **described** by Appellants, **not** that the specific polymorphisms **identified** and **described** by Appellants are "potential" polymorphisms. Thus, the Examiner's argument completely fails to support the alleged lack of utility, and taken with the admission that "forensic analysis can be useful for determining the presence or absence of polymorphisms which (*sic*) have been demonstrated to exist" (the Examiner's Answer at page 7), actually suggests that the presently claimed sequences meet the requirements of 35 U.S.C. § 101.

In view of the facts presented above, Appellants respectfully point out that the Examiner's position

concerning the statements in the specification **completely** defies logic, and in no way meets the Examiner's burden of establishing that those skilled in the art would not believe the presently claimed sequence has the utility asserted by Appellants. In conclusion, Appellants submit that the use of the term "can" in the section of the specification quoted by the Examiner in **no way** suggests to the skilled artisan that the polymorphic markers **identified** and **described** by Appellants are merely "potential" polymorphic markers, and point out that the use of the term "can" is completely proper when considered in the above context.

Additionally, Appellants pointed out in the Appeal Brief that a sequence sharing 100% identity at the protein level over an extended region of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists at the National Center for Biotechnology Information who are *wholly unaffiliated with Appellants* as a "serine protease" (GenBank accession number XM_171629; see **Exhibit A** in the Appeal Brief), and that an additional sequence sharing almost 100% percent identity at the amino acid level over an even greater length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has also been annotated by third party scientists *wholly unaffiliated with Appellants* as a "serine protease" (GenBank accession number XM_208689; see **Exhibit B** in the Appeal Brief). The Examiner continues to question Appellants' assertion that the presently claimed sequence encodes a human serine protease, citing articles by Attwood and Miller (*Comput. Chem.* **25**:329-339, 2001) and Ponting (*Brief. Bioinform.* **2**:19-29, 2001) in an attempt to support this position.

Appellants first pointed out that the PTO has repeatedly attempted to deny the utility of nucleic acid sequences based on a small number of spurious publications that call into doubt the usefulness of bioinformatic predictions, of which these two articles are merely the latest examples. The Examiner states that "(t)he cited references of Attwood et al. and Ponting are not spurious publications because the references provide rational and scientific explanations" (the Examiner's Answer at page 8). Appellants respectfully point out that the references cited by the Examiner (as well as a handful of other references cited by the PTO in the context of rejections under 35 U.S.C. § 101) are in fact "spurious", in that there are hundreds if not **thousands** of journal articles, which also use "rational and scientific explanations", to **support** Appellants' position that the overwhelming majority of those of skill in the relevant art would

believe prediction of protein function from homology information and the usefulness of bioinformatic predictions to be powerful and useful tools. Appellants respectfully point out that the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be **believable**. As **believability** is the standard for meeting the utility requirement of 35 U.S.C. § 101, and **not** 100% consensus or 100% accuracy, Appellants submit that, given the numerous references that support Appellants' assertion, as well as these two GenBank annotations by third party scientists, the present claims must clearly meet the requirements of 35 U.S.C. § 101.

Appellants further pointed out that while they agree that there is not 100% consensus within the scientific community regarding prediction of protein function from homology information, and further agree that prediction of protein function from homology information is not 100% accurate, the lack of 100% consensus on prediction of protein function from homology information is **completely irrelevant** to the question of whether the claimed nucleic acid sequence has a substantial and specific utility, and that 100% accuracy of prediction of protein function from homology information is **not the standard** for patentability under 35 U.S.C. § 101. Appellants respectfully point out Peter Duesberg, a member of the National Academy of Science, has published a number of papers in which he argues that the HIV virus is not the cause of AIDS. However, citation of these references does not serve to prove that those of skill in the art do not believe that HIV causes AIDS. Likewise, the citation of a few articles that question prediction of protein function from homology information is not indicative of what a substantial number of skilled artisans believe concerning prediction of protein function from homology information, and therefore does **not** support an allegation that the presently claimed sequences lack a patentable utility. Without evidence that a substantial number of those of skill in the art would not believe Appellants' assertion that the presently claimed sequence encodes a serine protease, the Examiner's argument fails to support the alleged lack of utility. Furthermore, in addition to the references cited by the Examiner not providing a general consensus that those of skill in the art do not believe prediction of protein function from homology information, the references cited by the Examiner to not speak **at all** to the specific sequences claimed by Appellants. Thus, while Appellants have provided evidence of record that conclusively establishes that those skilled in the art would believe that the specifically claimed sequence encodes a serine protease, the Examiner has

provided no evidence that directly establishes that the specifically claimed sequence does not encode a serine protease. Accordingly, the evidence of record compels a finding that the present invention has a patentable utility.

Furthermore, with regard to references that teach that slight variation in amino acid sequence can lead to proteins with different functions, Appellants pointed out that the **PTO itself** does not require 100% identity between proteins to establish functional homology. Example 10 of the Revised Interim Utility Guidelines Training Materials only requires a similarity score greater than 95% to establish functional homology. Thus, scientific publications that generally assert that very small changes between amino acid sequences can lead to changes in function, or publications describing specific examples of proteins, distinct from Appellants sequence, where a minor change in amino acid sequence has lead to a change in function, have been viewed by the PTO itself as **irrelevant** to the question of utility, and thus do not support the Examiner's allegation that the presently claimed sequence lacks utility. Therefore, the present utility rejection must fail as a matter of policy, as a matter of science, and as a matter of law.

Furthermore, Appellants detailed additional examples of the utility of the present nucleotide sequences, such as in assessing gene expression patterns using high-throughput DNA chips, and in determining the genomic structure of the protein encoding regions of the corresponding human chromosome. The Examiner continues to question these assertions of utility, because "any new polynucleotide" can be used in these applications (the Examiner's Answer at page 9). Appellants pointed out in the Appeal Brief that these arguments are flawed in a number of respects. However, Appellants wish to emphasize one important point that has **never** been addressed by the Examiner. Appellants once again respectfully point out that the Examiner is clearly confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. As **clearly** stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Thus, the quote above clearly establishes that the fact that **other** polynucleotides can be used in assessing gene expression patterns and determining the genomic structure of the protein coding regions of the corresponding human chromosome are completely irrelevant in assessing the requirements under 35 U.S.C. § 101. The **only** relevant enquiry with regard to patentability under 35 U.S.C. § 101 is whether **every** polynucleotide can be used in assessing gene expression patterns and determining the genomic structure of the protein coding regions of the corresponding human chromosome, and the answer is an emphatic **no**. Importantly, the holding in *Carl Zeiss* is **mandatory legal authority** that is directly applicable to the present appeal, and **directly** rebuts the Examiner's argument. Appellants further pointed out that the requirement for a unique utility is not only in conflict with established case law, it is also not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. **All** batteries have the **exact same** utility - specifically, to provide power. **All** automobile tires have the **exact same** utility - specifically, for use on automobiles. **All** golf balls and golf clubs have the **exact same** utility - specifically, use in the game of golf. **All** cancer treatments have the **exact same** utility - specifically, to treat cancer. **All** anti-infectious agents have the **exact same** broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

For each of the foregoing reasons, as well as the reasons set forth in the Appeal Brief, Appellants submit that the rejection of claims 1, 2 and 5-10 under 35 U.S.C. § 101 must be overruled.

B. Are Claims 1, 2 and 5-10 Unusable Due to a Lack of Patentable Utility?

Regarding the rejection of claims 1, 2 and 5-10 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility, Appellants submit that as claims 1, 2 and 5-10 have been shown to have "a specific, substantial, and credible utility", as detailed in Section X(A) above, as well as Section VIII(A) of the Appeal Brief, the present rejection of claims 1, 2 and 5-10 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1, 2 and 5-10 under 35 U.S.C. § 112, first paragraph, must be overruled.

C. Do Claims 1 and 7-10 Lack Sufficient Written Description?

Appellants do not wish to restate all of the arguments presented in the Appeal Brief concerning the Examiner's allegation that claims 1 and 7-10 contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, and instead incorporate the entirety of Section VIII(C) of the Appeal Brief at this point herein by reference. However, Appellants are compelled to specifically address certain arguments presented in the Examiner's Answer for the record.

The Examiner continues to insist that the present claims lack sufficient written description support because the claims "encompass a wide breadth of polynucleotides with biological functions that have yet to be discovered" (the Examiner's Answer at page 11). Appellants once again respectfully point out that there is **no requirement whatsoever** that novel fragments of a novel sequence have the **exact same function** as the full length sequence in order to be patented. If this were to be the case, hundreds, if not thousands, of issued U.S. Patents would be instantly invalidated, as they each claim nucleotide fragments that have not been demonstrated to have the exact same function as the full length nucleotide sequence. Appellants therefore submit that the claimed sequence meets the written description requirement of 35 U.S.C. § 112, first paragraph.

Additionally, the Examiner states that claims 1 and 7-10 do not meet the written description

requirements because "the instant application only discloses only (*sic*) one species encompassed by the claim: a polynucleotide consisting of a nucleotide sequence of SEQ ID NO:3" (the Examiner's Answer at page 11). Appellants respectfully disagree, and simply point out that SEQ ID NO:3, which the Examiner admits is disclosed in the instant application, **alone** discloses **well over 1000 species** (over 900 60-mers alone) that are encompassed by claim 1 ("[A]n isolated nucleic acid molecule comprising at least 60 contiguous nucleotides from SEQ ID NO:3"). Thus, the Examiner's argument fails to support the allegation that claims 1, 7 and 10 lack sufficient written description support.

Finally, the Examiner has not commented **at all** on any of the case law cited by Appellants that supports Appellants assertion that the present claims meet the written description requirement of 35 U.S.C. § 112, first paragraph. Appellants wish to emphasize the holding of one case in particular for the record. Recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Regents of Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Regents of Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the

sequence itself, the present claims meet the written description requirement of 35 U.S.C. § 112, first paragraph.

Using the nucleic acid sequences of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to **distinguish** the claimed nucleic acids from other materials on the basis of the specific **structural** description provided. Polynucleotides comprising at least 60 contiguous bases from SEQ ID NO:3 are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. The claimed genus of polynucleotides is clearly defined in structural terms, which is **all that is required** of claims 1 and 7-10 to meet the written description requirement of 35 U.S.C. § 112, first paragraph (*Regents of Univ. of California v. Eli Lilly and Co., supra*).

Nevertheless, while in no way agreeing with the present rejection, should this rejection be maintained through all levels of appeal available to Appellants, and should this issue be the sole impediment to patentability of the present claims, Appellants hereby state that a deposit of the original clone containing SEQ ID NO:3 would be made to the American Type Culture Collection (ATCC), thus removing all question of whether the claims meet the written description requirement. It is well established through years of court decisions, and recently confirmed by the Federal Circuit in *Enzo Biochem, Inc. v. Gen-Probe, Inc.* (296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002)), a deposit of biological material with the ATCC can be used to satisfy the written description requirement.

For each of the foregoing reasons, Appellants submit that the rejection of claims 1 and 7-10 under 35 U.S.C. § 112, first paragraph, must be overruled.

XI. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, as well as the arguments set forth in the Appeal Brief, the conclusion that claims 1, 2 and 5-10 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility, and that claims 1 and 7-10 are not enabled and lack sufficient written description, is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

February 4, 2004
Date

David W. Hibler Reg. No. 41,071
Agent For Appellants

LEXICON GENETICS INCORPORATED
8800 Technology Forest Place
The Woodlands, TX 77381
(281) 863-3399

Customer # 24231

TABLE OF AUTHORITIES

CASES

STATUTES

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Walke *et al.*		
Serial No.:	09/755,016	Group Art Unit:	1652
Filed:	01/05/2001	Examiner:	C. Fronda
For:	Novel Human Proteases and Polynucleotides Encoding the Same	Attorney Docket No.:	LEX-0114-USA

REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TABLE OF CONTENTS

APPEAL BRIEF

Sir:

Appellants hereby submit an original and two copies of this Reply Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Examiner's Answer mailed on December 4, 2003. This Reply Brief is timely submitted, and Appellants believe no fees are due in connection with this Reply Brief. However, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

Appellants agree with the Examiner's assertion that "(a) statement identifying the real party in interest is contained in the brief" (Examiner's Answer at page 1).

II. RELATED APPEALS AND INTERFERENCES

Appellants agree with the Examiner's assertion that "(t)he brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief" (Examiner's Answer at page 2).

III. STATUS OF THE CLAIMS

Appellants agree with the Examiner's assertion that "(t)he statement of the status of the claims contained in the brief is correct" (Examiner's Answer at page 2).

IV. STATUS OF THE AMENDMENTS

Appellants agree with the Examiner's assertion that "(t)he appellant's statement of the status of amendments after final rejection contained in the brief is correct" (Examiner's Answer at page 2).

V. SUMMARY OF THE INVENTION

Appellants agree with the Examiner's assertion that "(t)he summary of invention contained in the brief is correct" (Examiner's Answer at page 2).

VI. ISSUES ON APPEAL

Appellants agree with the Examiner's assertion that "(t)he appellant's statement of the issues in the brief is correct" (Examiner's Answer at page 2).

VII. GROUPING OF THE CLAIMS

Appellants disagree with the Examiner's assertion that "Appellant's brief includes a statement that claims 1, 2, and 5-10 do not stand or fall together" (Examiner's Answer at page 2). Appellants clearly stated in the Appeal Brief, and reiterate here, that "(f)or the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, associated with the utility rejection, the claims will stand or fall together. For the purposes of the outstanding rejection under 35 U.S.C. § 112, first paragraph, associated with written description, claims 1 and 7-10 will stand or fall together."

VIII. CLAIMS APPEALED

Appellants agree with the Examiner's assertion that "(t)he copy of the appealed claims contained in the Appendix to the brief is correct" (Examiner's Answer at page 2).

IX. PRIOR ART OF RECORD

Appellants agree with the Examiner's assertion that "Attwood et al." and "Ponting" are the only prior art references of record relied on in the currently pending rejections (Examiner's Answer bridging pages 2 and 3).

X. ARGUMENT

A. Do Claims 1, 2 and 5-10 Lack a Patentable Utility?

Appellants do not wish to restate all of the arguments presented in the Appeal Brief concerning the Examiner's allegation that claims 1, 2 and 5-10 lack a patentable utility, and instead incorporate the entirety of Section VIII(A) of the Appeal Brief at this point herein by reference. However, Appellants are compelled to specifically address certain arguments presented in the Examiner's Answer for the record.

Appellants pointed out in the Appeal Brief that the present nucleic acid sequences have utility in forensic analysis, as described in the specification as originally filed (see, for example, page 10, lines 13-24). As described in the specification at page 15, lines 22-29, the presently claimed sequence defines three coding single nucleotide polymorphisms - specifically, a C/T polymorphism at nucleotide position 28 of SEQ ID NO:3, a silent polymorphism that results in a leucine at amino acid position 10 of SEQ ID NO:4; a C/T polymorphism at nucleotide position 55 of SEQ ID NO:3, which can result in a tyrosine or histidine at amino acid position 19 of SEQ ID NO:4; and a G/A polymorphism at nucleotide position 379 of SEQ ID NO:3, which can result in an alanine or threonine at amino acid position 127 of SEQ ID NO:4. Appellants pointed out that as such polymorphisms are the basis for forensic analysis, which in undoubtedly a "real world" utility, the presently claimed sequence must in itself be useful.

In the Examiner's Answer, the Examiner states that "forensic analysis can be useful for determining the presence or absence of polymorphisms which (*sic*) have been demonstrated to exist" (the Examiner's Answer at page 7), but then states that the polymorphic markers **identified** and **described** by Appellants in the specification as originally filed are not useful in forensic analysis because "the instant specification only describes **potential** polymorphisms but not actual polymorphisms" (the Examiner's Answer at page 7, emphasis in original). The Examiner appears to believe that the polymorphic markers **identified** and **described** by Appellants in the specification as originally filed are not "actual" polymorphisms because of the use of the word "can" by Appellants: "the specification states on page 15, lines 22-30: 'the described NHP sequences **can** contain a variety of polymorphisms such as at nucleotide 28 of SEQ ID NO:3 and nucleotide 55 of SEQ ID NO:3 which both can be a C or a T and **can** give rise to silent mutation at corresponding amino acid position 10 of SEQ ID NO:4 or a tyr or his at amino acid position 19 of SEQ

ID NO:4. The described NHP sequences can also contain G-A polymorphisms at nucleotide 379 of SEQ ID NO:3 and nucleotide position 199 of SEQ ID NO:5 which **can** give rise to a corresponding ala or thr at amino acid position 127 of SEQ ID NO:4, or residue 67 of SEQ ID NO:6.' (emphasis added)" (the Examiner's Answer at page 6, emphasis in original).

First, it should be pointed out that the section of the specification quoted by the Examiner refers to "sequences", specifically, the claimed SEQ ID NOS:3 and 4. Appellants respectfully point out that nucleotide and amino acid sequences in and of themselves cannot contain a polymorphism - rather, a polymorphism is a representation of a position in a population of nucleotide sequences that exhibits variability within a number of independent isolates of a given sequence. Thus, any specific nucleotide sequence, for example SEQ ID NO:3, **can** have either the first or the second nucleotide at the polymorphic position, not both. The same holds true for the specifically claimed amino acid sequence (SEQ ID NO:4); the amino acid sequence **can** have either the first or the second amino acid at the polymorphic position, not both. Thus, the word "can", as used by Appellants in this context, means the possibility of the first nucleotide or amino acid or the second nucleotide or amino acid, **not** that the specific polymorphisms **identified** and **described** by Appellants are "potential" polymorphisms.

Second, the use of the term "can" in the context of the statement "the described NHP sequences can contain a variety of polymorphisms such as" those **identified** and **described** by Appellants also means that "the described NHP sequences" **can** contain other polymorphisms in addition to those **identified** and **described** by Appellants, including any previously identified polymorphisms, and any polymorphisms that might be identified in the future. Thus, the word "can", as used by Appellants in this context, means the possibility of the claimed sequences containing other polymorphisms in addition to those **identified** and **described** by Appellants, **not** that the specific polymorphisms **identified** and **described** by Appellants are "potential" polymorphisms. Thus, the Examiner's argument completely fails to support the alleged lack of utility, and taken with the admission that "forensic analysis can be useful for determining the presence or absence of polymorphisms which (*sic*) have been demonstrated to exist" (the Examiner's Answer at page 7), actually suggests that the presently claimed sequences meet the requirements of 35 U.S.C. § 101.

In view of the facts presented above, Appellants respectfully point out that the Examiner's position

concerning the statements in the specification **completely** defies logic, and in no way meets the Examiner's burden of establishing that those skilled in the art would not believe the presently claimed sequence has the utility asserted by Appellants. In conclusion, Appellants submit that the use of the term "can" in the section of the specification quoted by the Examiner in **no way** suggests to the skilled artisan that the polymorphic markers **identified** and **described** by Appellants are merely "potential" polymorphic markers, and point out that the use of the term "can" is completely proper when considered in the above context.

Additionally, Appellants pointed out in the Appeal Brief that a sequence sharing 100% identity at the protein level over an extended region of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists at the National Center for Biotechnology Information who are *wholly unaffiliated with Appellants* as a "serine protease" (GenBank accession number XM_171629; see **Exhibit A** in the Appeal Brief), and that an additional sequence sharing almost 100% percent identity at the amino acid level over an even greater length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has also been annotated by third party scientists *wholly unaffiliated with Appellants* as a "serine protease" (GenBank accession number XM_208689; see **Exhibit B** in the Appeal Brief). The Examiner continues to question Appellants' assertion that the presently claimed sequence encodes a human serine protease, citing articles by Attwood and Miller (*Comput. Chem.* **25**:329-339, 2001) and Ponting (*Brief. Bioinform.* **2**:19-29, 2001) in an attempt to support this position.

Appellants first pointed out that the PTO has repeatedly attempted to deny the utility of nucleic acid sequences based on a small number of spurious publications that call into doubt the usefulness of bioinformatic predictions, of which these two articles are merely the latest examples. The Examiner states that "(t)he cited references of Attwood et al. and Ponting are not spurious publications because the references provide rational and scientific explanations" (the Examiner's Answer at page 8). Appellants respectfully point out that the references cited by the Examiner (as well as a handful of other references cited by the PTO in the context of rejections under 35 U.S.C. § 101) are in fact "spurious", in that there are hundreds if not **thousands** of journal articles, which also use "rational and scientific explanations", to **support** Appellants' position that the overwhelming majority of those of skill in the relevant art would

believe prediction of protein function from homology information and the usefulness of bioinformatic predictions to be powerful and useful tools. Appellants respectfully point out that the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be **believable**. As **believability** is the standard for meeting the utility requirement of 35 U.S.C. § 101, and **not** 100% consensus or 100% accuracy, Appellants submit that, given the numerous references that support Appellants' assertion, as well as these two GenBank annotations by third party scientists, the present claims must clearly meet the requirements of 35 U.S.C. § 101.

Appellants further pointed out that while they agree that there is not 100% consensus within the scientific community regarding prediction of protein function from homology information, and further agree that prediction of protein function from homology information is not 100% accurate, the lack of 100% consensus on prediction of protein function from homology information is **completely irrelevant** to the question of whether the claimed nucleic acid sequence has a substantial and specific utility, and that 100% accuracy of prediction of protein function from homology information is **not the standard** for patentability under 35 U.S.C. § 101. Appellants respectfully point out Peter Duesberg, a member of the National Academy of Science, has published a number of papers in which he argues that the HIV virus is not the cause of AIDS. However, citation of these references does not serve to prove that those of skill in the art do not believe that HIV causes AIDS. Likewise, the citation of a few articles that question prediction of protein function from homology information is not indicative of what a substantial number of skilled artisans believe concerning prediction of protein function from homology information, and therefore does **not** support an allegation that the presently claimed sequences lack a patentable utility. Without evidence that a substantial number of those of skill in the art would not believe Appellants' assertion that the presently claimed sequence encodes a serine protease, the Examiner's argument fails to support the alleged lack of utility. Furthermore, in addition to the references cited by the Examiner not providing a general consensus that those of skill in the art do not believe prediction of protein function from homology information, the references cited by the Examiner to not speak **at all** to the specific sequences claimed by Appellants. Thus, while Appellants have provided evidence of record that conclusively establishes that those skilled in the art would believe that the specifically claimed sequence encodes a serine protease, the Examiner has

provided no evidence that directly establishes that the specifically claimed sequence does not encode a serine protease. Accordingly, the evidence of record compels a finding that the present invention has a patentable utility.

Furthermore, with regard to references that teach that slight variation in amino acid sequence can lead to proteins with different functions, Appellants pointed out that the **PTO itself** does not require 100% identity between proteins to establish functional homology. Example 10 of the Revised Interim Utility Guidelines Training Materials only requires a similarity score greater than 95% to establish functional homology. Thus, scientific publications that generally assert that very small changes between amino acid sequences can lead to changes in function, or publications describing specific examples of proteins, distinct from Appellants sequence, where a minor change in amino acid sequence has lead to a change in function, have been viewed by the PTO itself as **irrelevant** to the question of utility, and thus do not support the Examiner's allegation that the presently claimed sequence lacks utility. Therefore, the present utility rejection must fail as a matter of policy, as a matter of science, and as a matter of law.

Furthermore, Appellants detailed additional examples of the utility of the present nucleotide sequences, such as in assessing gene expression patterns using high-throughput DNA chips, and in determining the genomic structure of the protein encoding regions of the corresponding human chromosome. The Examiner continues to question these assertions of utility, because "any new polynucleotide" can be used in these applications (the Examiner's Answer at page 9). Appellants pointed out in the Appeal Brief that these arguments are flawed in a number of respects. However, Appellants wish to emphasize one important point that has **never** been addressed by the Examiner. Appellants once again respectfully point out that the Examiner is clearly confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. As **clearly** stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Thus, the quote above clearly establishes that the fact that **other** polynucleotides can be used in assessing gene expression patterns and determining the genomic structure of the protein coding regions of the corresponding human chromosome are completely irrelevant in assessing the requirements under 35 U.S.C. § 101. The **only** relevant enquiry with regard to patentability under 35 U.S.C. § 101 is whether **every** polynucleotide can be used in assessing gene expression patterns and determining the genomic structure of the protein coding regions of the corresponding human chromosome, and the answer is an emphatic **no**. Importantly, the holding in *Carl Zeiss* is **mandatory legal authority** that is directly applicable to the present appeal, and **directly** rebuts the Examiner's argument. Appellants further pointed out that the requirement for a unique utility is not only in conflict with established case law, it is also not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. **All** batteries have the **exact same** utility - specifically, to provide power. **All** automobile tires have the **exact same** utility - specifically, for use on automobiles. **All** golf balls and golf clubs have the **exact same** utility - specifically, use in the game of golf. **All** cancer treatments have the **exact same** utility - specifically, to treat cancer. **All** anti-infectious agents have the **exact same** broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

For each of the foregoing reasons, as well as the reasons set forth in the Appeal Brief, Appellants submit that the rejection of claims 1, 2 and 5-10 under 35 U.S.C. § 101 must be overruled.

B. Are Claims 1, 2 and 5-10 Unusable Due to a Lack of Patentable Utility?

Regarding the rejection of claims 1, 2 and 5-10 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility, Appellants submit that as claims 1, 2 and 5-10 have been shown to have "a specific, substantial, and credible utility", as detailed in Section X(A) above, as well as Section VIII(A) of the Appeal Brief, the present rejection of claims 1, 2 and 5-10 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1, 2 and 5-10 under 35 U.S.C. § 112, first paragraph, must be overruled.

C. Do Claims 1 and 7-10 Lack Sufficient Written Description?

Appellants do not wish to restate all of the arguments presented in the Appeal Brief concerning the Examiner's allegation that claims 1 and 7-10 contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, and instead incorporate the entirety of Section VIII(C) of the Appeal Brief at this point herein by reference. However, Appellants are compelled to specifically address certain arguments presented in the Examiner's Answer for the record.

The Examiner continues to insist that the present claims lack sufficient written description support because the claims "encompass a wide breadth of polynucleotides with biological functions that have yet to be discovered" (the Examiner's Answer at page 11). Appellants once again respectfully point out that there is **no requirement whatsoever** that novel fragments of a novel sequence have the **exact same function** as the full length sequence in order to be patented. If this were to be the case, hundreds, if not thousands, of issued U.S. Patents would be instantly invalidated, as they each claim nucleotide fragments that have not been demonstrated to have the exact same function as the full length nucleotide sequence. Appellants therefore submit that the claimed sequence meets the written description requirement of 35 U.S.C. § 112, first paragraph.

Additionally, the Examiner states that claims 1 and 7-10 do not meet the written description

requirements because "the instant application only discloses only (*sic*) one species encompassed by the claim: a polynucleotide consisting of a nucleotide sequence of SEQ ID NO:3" (the Examiner's Answer at page 11). Appellants respectfully disagree, and simply point out that SEQ ID NO:3, which the Examiner admits is disclosed in the instant application, **alone** discloses **well over 1000 species** (over 900 60-mers alone) that are encompassed by claim 1 ("[A]n isolated nucleic acid molecule comprising at least 60 contiguous nucleotides from SEQ ID NO:3"). Thus, the Examiner's argument fails to support the allegation that claims 1, 7 and 10 lack sufficient written description support.

Finally, the Examiner has not commented **at all** on any of the case law cited by Appellants that supports Appellants assertion that the present claims meet the written description requirement of 35 U.S.C. § 112, first paragraph. Appellants wish to emphasize the holding of one case in particular for the record. Recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Regents of Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Regents of Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the

sequence itself, the present claims meet the written description requirement of 35 U.S.C. § 112, first paragraph.

Using the nucleic acid sequences of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to **distinguish** the claimed nucleic acids from other materials on the basis of the specific **structural** description provided. Polynucleotides comprising at least 60 contiguous bases from SEQ ID NO:3 are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. The claimed genus of polynucleotides is clearly defined in structural terms, which is **all that is required** of claims 1 and 7-10 to meet the written description requirement of 35 U.S.C. § 112, first paragraph (*Regents of Univ. of California v. Eli Lilly and Co., supra*).

Nevertheless, while in no way agreeing with the present rejection, should this rejection be maintained through all levels of appeal available to Appellants, and should this issue be the sole impediment to patentability of the present claims, Appellants hereby state that a deposit of the original clone containing SEQ ID NO:3 would be made to the American Type Culture Collection (ATCC), thus removing all question of whether the claims meet the written description requirement. It is well established through years of court decisions, and recently confirmed by the Federal Circuit in *Enzo Biochem, Inc. v. Gen-Probe, Inc.* (296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002)), a deposit of biological material with the ATCC can be used to satisfy the written description requirement.

For each of the foregoing reasons, Appellants submit that the rejection of claims 1 and 7-10 under 35 U.S.C. § 112, first paragraph, must be overruled.

XI. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, as well as the arguments set forth in the Appeal Brief, the conclusion that claims 1, 2 and 5-10 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility, and that claims 1 and 7-10 are not enabled and lack sufficient written description, is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

February 4, 2004
Date

David W. Hibler Reg. No. 41,071
Agent For Appellants

LEXICON GENETICS INCORPORATED
8800 Technology Forest Place
The Woodlands, TX 77381
(281) 863-3399

Customer # 24231

TABLE OF AUTHORITIES

CASES

STATUTES